

ACR 2006 Atacicept SLE abstract

Title: Trial of Atacicept in Patients with Systemic Lupus Erythematosus (SLE)

Category: 25. SLE - clinical aspects and treatment

Author(s): Maria Dall'Era¹, Eliza Chakravarty², Mark Genovese², Daniel Wallace³, Arthur Kavanaugh⁴, Kenneth Kalunian⁴, Patricia Dhar⁵, Claudia Pena-Rossi⁶, David Wofsy¹, Serono and ZymoGenetics Atacicept Study Group. ¹University of California, San Francisco, CA; ²Stanford University, Palo Alto, CA; ³Cedars-Sinai Medical Center, Los Angeles, CA; ⁴University of California, San Diego, CA; ⁵Wayne State University, Detroit, MI; ⁶Serono, Geneva, Switzerland

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Purpose: To assess the safety, pharmacokinetics, and pharmacodynamics of atacicept in SLE patients. Atacicept is a TACI-Ig fusion protein that inhibits B cell stimulation by binding to BLyS and APRIL.

Methods: This study was a phase Ib double-blind, placebo-controlled, dose-escalating trial. 6 cohorts comprised of 8 SLE patients each were treated with atacicept or placebo in a 3:1 ratio. Cohorts 1-4 received a single subcutaneous dose of 0.3, 1, 3, or 9 mg/kg of atacicept. Cohorts 5-6 received four weekly doses of 1 mg/kg or 3 mg/kg. Patients were followed for 6 weeks (cohorts 1-4) or 9 weeks (cohorts 5-6).

Results: Forty-nine patients with mild-moderate SLE were enrolled. Biological activity of atacicept was demonstrated by dose-dependent reductions in immunoglobulin levels and in total and mature B cells. This effect was most pronounced in the multiple dose cohorts. By day 36, median IgM levels declined by nearly 50% in the 3 mg/kg group compared with 30% in the 1 mg/kg group and 4% in the placebo group. Median IgG and IgA levels declined by 16% and 32%, respectively, in the high dose groups.

Flow cytometry revealed a reduction in total and mature B cells in the single and multiple dose cohorts. In both repeat dose cohorts, total B cells declined by 30-35% and mature B cells declined by 50-60% relative to baseline. These effects were sustained through the 9-week follow-up period. There were no changes in the number of T cells, NK cells, or monocytes.

Mild injection site reactions occurred more frequently among treated patients than controls. There were no differences in the frequency or type of adverse events (AEs), including infections, between the placebo and atacicept groups and no severe or serious AEs in patients treated with atacicept. Treated patients maintained protective levels of anti-tetanus antibodies.

Although this study was not powered to assess efficacy, the following observations were encouraging. 8 patients had low complement levels at baseline. Six of these patients received either placebo or a single dose of atacicept, and all of them had low complement at the end of the study. Two patients with low complement received multiple doses of atacicept, and both of them had normal complement by the end of the study. Also, among the 6 patients with a SLEDAI score of ≥ 6 at baseline, the 3 treated with placebo did not improve whereas 2/3 atacicept patients achieved scores of 0 at the end of follow-up.

Conclusion: Atacicept administered subcutaneously was well-tolerated and demonstrated biological activity consistent with the proposed mechanism of action. These results indicate that atacicept warrants further investigation as a therapeutic agent.

Disclosures: M. Dall'Era, Serono, 2; E. Chakravarty, Serono, 2; M. Genovese, Serono, 2; D. Wallace, Serono, 2; A. Kavanaugh, Serono, 2; K. Kalunian, Serono, 2; P. Dhar, Serono,

2; **C. Pena-Rossi**, Serono, 1; **D. Wofsy**, Serono, 2.